REMARKS/ARGUMENTS

Claims 26 and 34 are cancelled. New claims 38 and 39 are added. Claims 21-25 27-33, and 35-37 are amended.

Applicant hereby submits a copy of proof for the hybridom cell line deposit.

Reconsideration is respectfully requested in view of the above amendments and the following remarks.

Rejection under 35 U.S.C. 112, second paragraph:

The Examiner rejects claims 29-32 and 34-37 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention under 35 USC 112, second paragraph. More specifically, the Examiner stated that the word "means" used in the claims is unclear as to whether it "refers to a method by which a tumor is targeted or a method by which an anti-tumor prodrug is activated or whether the term "means" refers to an actual agent, such as an antibody for the tumor targeting or an enzyme for the activation of a prodrug."

Applicants have amended the term "means" to "moiety", which makes clear that it does not refer to a method. Accordingly, rejection under 35 USC 112, second paragraph, is obviated.

Rejection under 35 U.S.C. 112, first paragraph:

The Examiner rejects claims 21-36 under 35 USC 112, first paragraph, as failing to comply with the written description requirement on the ground that the specification describes the accelerated clearance of only two polyethylene glycol-containing compounds while the claims claim cover a genus of polyethylene glycol-containing compounds. Applicants respectfully disagree.

As the Examiner pointed out, a description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus ***or by describing structural features common to the genus that constitute a substantial portion of genus***. *See University of California v. Eli Lilly and Co.,* 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406. The present invention is directed to using an anti-polyethylene glycol (PEG) antibody to remove PEG-containing compounds in the blood circulation. The common structural feature of these PEG-containing compounds is PEG. PEG is the only portion in the PEG-containing compounds relevant to the present invention because the antibody is specific to PEG. Thus, any compound in the blood circulation that has a PEG portion can be bound by the antibody, irrespective of what the other portions of the targeted compound are. Normally, this antigen (PEG) and antibody relationship will not be altered by the nature of other parts of a PEG-containing compound. A person of ordinary skill in the art would expect that the antibody binds one PEG-containing compound will bind the other as well. There is no basis to assume otherwise.

The written description requirement only requires a patentee to sufficiently describe the *invention*. There is no such requirement that an application describe every detail unrelated to the invention. Here, the invention is to use an anti-PEG antibody to remove PEG-containing compounds in the blood circulation, not the compound per se. Applicants have described the effectiveness of an anti-PEG antibody in removing certain PEG-containing compounds, of which the Examiner does not argue the adequacy. It is unnecessary to describe other PEG-containing compounds as the PEG portions of all such compounds are the same and can be logically concluded that those other PEG-containing can be removed in the same manner based on the common knowledge about antibody-antigen reaction. Thus, the written description requirement

is satisfied. Applicants respectfully submit that the rejection to claims 21-36 under 35 USC 112, first paragraph, has been overcome and should be withdrawn.

Rejection under 35 USC 102

The Examiner rejects claims 21-28 under 35 USC 102(a) as being anticipated by Cheng et al. (Bioconjugate Chem. 1999; 10:520-528).

The Cheng reference has five authors, of whom three are named as co-inventors of the present application. Co-authors of the Cheng reference Ming-Fang Wu and Ji-Wang Chern are not co-inventors of the present invention.

Applicants hereby submit a Declaration, dated February 21, 2002, of Dr. Steve R. Roffler, a co-inventor of the present application and the corresponding author of the Cheng reference. This declaration was submitted in the U.S. Patent Application, Serial No. 09/520,255, filed March 7, 2000, of which the present application is a divisional. Dr. Roffler verifies that the two co-authors of the Cheng reference who were not named as the co-inventors in the present application did not make any intellectual contributions to the claimed invention. According to Dr. Roffler, they were co-authors of the Cheng reference because one of them made tissue sections of the livers, kidneys and spleens of drug-treated mice and subsequently examined the tissue sections for organ pathology, and the other provided laboratory space and direction on the synthesis of glucuronide prodrug BHAMG.

Claim 21-28 are directed to a method for accelerating the clearance of a polyethylene glycol-containing compound in the blood circulation by administering to the patient an anti-polyethylene glycol-containing monoclonal antibody. It has nothing to do with the preparation of the prodrug. Since none of the works performed by these two authors relates to the presently claimed invention, they simply cannot be considered as co-inventors of the claimed invention.

Accordingly, the reference Cheng et al. should be removed as prior art. It is respectfully submitted that the rejection to claims 21-28 under 35 USC 102(a) has been overcome and should be withdrawn.

Rejection under 35 U.S.C. 103(a)

The Examiner rejects claims 29-37 under 35 USC 103(a) as being unpatentable over Cheng et al. (Cancer Imunol. Immunother. 1997; 44:305-315) in combination with Cheng et al. (Bioconjugate Chem. 1999; 10:520-528).

Cheng et al. (Bioconjugate Chem. 1999; 10:520-528) has been discussed above in connection with the section 102 rejection. For the same reason, this reference is not a proper prior art reference to the present invention. Absent this reference, Cheng et al. (Cancer Imunol. Immunother. 1997; 44:305-315) alone cannot render claims 29-37 obvious. Thus, rejection to claims 29-37 under 35 USC 103(a) has been overcome and should be withdrawn.

The Examiner also rejects claims 21-25, 28-33 and 36-37 under 35 USC 103(a) as being unpatentable over Griffiths et al. (U.S. Pat. 6,077,499) in combination with Richter et al. (Int. Archs Allergy Appl. Immun. 1983; 70: 124-131) in further view of Hershfield et al (Proc. Natl. Acad. Sci. 1991; 88: 7185-7189). Applicants respectfully disagree with the Examiner.

As the Examiner pointed out, Griffiths et al. describe clearing agents that are *anti-protein* (Mab) antibodies, and do not teach *anti-PEG monoclonal* antibodies. Nor do Griffiths et al. suggest that anti-PEG *monoclonal* antibodies be used as clearing agents in cancer therapy.

Similarly, neither Richter et al., which only teach how to make *anti-PEG polyclonoal* antibodies, nor Hershfield et al. which teach *anti-protein* antibodies, suggest that anti-PEG antibodies could result in the clearance of an immunoconjugate. It is an unwarranted leap to assume that an anti-PEG antibody would have the same effect as an antibody against a protein in

accelerating clearance of a pegylated protein, as the mechanism of clearance in blood circulation is still poorly understood and the results are highly unpredictable.

It is a requirement under 35 USC 103(a) that there must be specific teaching or suggestion in the prior art references to combine them when arguing obviousness relying on the combination of the references. In the above references, there is none. Absent any teaching or suggestion, a person of ordinary skill in the art, who is confronted with the same problem as applicants, would not be able to solve the problem in the same way as applicants did. Thus, claims 21-25, 28-33 and 36-37 are not obvious.

The Examiner further rejects claims 21-26, 28-34 and 36-37 under 35 USC 103(a) as being unpatentable over Griffiths et al. (U.S. Pat. 6,077,499) in combination with Richter et al. (Int. Archs Allergy Appl. Immun. 1983; 70: 124-131) in further view of Hershfield et al (Proc. Natl. Acad. Sci. 1991; 88: 7185-7189) in further view of Springer (US 4,427,653, 1984).

The first three cited references have been discussed above. Springer only teaches how to make monoclonal antibodies. Again, none of the cited references, alone or in combination, teach or suggest clearance of a toxin in the blood circulation by anti-PEG monoclonal antibodies. Absent such teaching or suggestion, the present invention cannot be viewed as being obvious under the law.

Accordingly, rejection to claims 21-26, 28-34 and 36-37 under 35 USC 103(a) has been overcome and should be withdrawn.

It is believed that no fees or charges are required at this time in connection with the present application. However, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,

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